sequences also encode a leader sequence for said single polypeptide wherein said leader sequence forms a secretion signal that is cleaved from said polypeptide following proteolytic processing.

REMARKS

The present invention stems from Applicants pioneering discovery that fully assembled antigen-specific immunoglobulin can be produced in a plant cell. The inventors also were the first to achieve a level of expression that makes possible passive immunization with plant produced antibodies. Plant produced antibodies are useful for systemic protection through administration i.v. as well as localized protection through local administration to a mucosal surface (e.g., lungs, digestive tract, nasopharyngeal cavity, the urogenital system).

The claims are generally directed to methods of passive immunization using a formulation comprising an antigen-specific immunoglobulin produced in transgenic plants. After amending the claims as set forth above, claims 13, 15-27, 29-82 will be pending in this application.

Applicants have amended claims 13, 41 and 66 to indicate that passive immunization is achieved with a formulation comprising an antigen specific immunoglobulin obtained by processing plant cells containing the requisite nucleotide sequences and antigen specific immunoglobulin product. The specification discusses various formulations and processing steps to prepare plant-derived immunoglobulin for use in passive immunization (see, e.g., page 38, line 30 to page 45, line 14). These amendments are designed to reflect the unique nature of antibody obtained from plants as compared to its natural source, mammalian cells. For example, a composition comprising plant derived immunoglobulin would be free from viral and proviral proteins or nucleic acid that necessarily is present to some extent as a contaminant in antibody compositions obtained from mammalian cells. Plant derived antibody compositions are safer for passive immunization from this perspective that would be mammalian cell derived antibody compositions. In addition, as described in the application (see page 44, lines 7-10) and well known in the art, mammalian glycoproteins that contaminate mammalian cell derived

immunoglobulin formulations would contain sialic acid while plant glycoproteins that contaminate plant cell derived immunoglobulin formulations would not.

Thus, in view of the above, the amendments raise no issue of new matter.

REJECTION UNDER 35 U.S.C. § 102 OVER STOLLE

The rejection of claims 13 and 15-30 under 35 U.S.C. § 102(b) as being allegedly anticipated by Stolle et al., (U.S. 4,748,018) is respectfully traversed. The Examiner is referred to the relevant sections of the Amendment filed March 13, 2002. In addition to those remarks, Applicants further note that a composition comprising an immunoglobulin derived from mammalian cells as taught by Stolle would contain viral or proviral proteins or such encoding nucleic acids as contaminants that necessarily are absent from plant derived immunoglobulin as taught by Applicants. In addition, glycoprotein contaminants in plant derived immunoglobulin would not contain sialic acid while such contaminants from mammalian derived immunoglobulin composition as described by Stolle would contain sialic acid. This latter point would also apply to forms of the antibody itself that contain glycosylation sites. Thus, the compositions of the instantly claimed methods are different.

REJECTION UNDER 35 U.S.C. § 103 OVER DÜRING IN VIEW OF STOLLE

The rejection of claims 13 and 15-30 under 35 U.S.C. § 103(a) as being allegedly unpatentable over a doctoral dissertation by Klaus During ("the During dissertation"), in view of Stolle et al, is respectively traversed. The Examiner is referred to the relevant sections of the Amendment filed March 13, 2002.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

Atty. Dkt. No.: EPI3007F
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The Examiner is urged to contact the undersigned by telephone to address any outstanding issues standing in the way of an allowance.

Respectfully submitted,

By _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

13. (Amended three times) A method of passively immunizing a human or non-human animal subject against a preselected antigen, said method comprising administering to said subject a prophylactic amount of **a formulation comprising** an antigen-specific immunoglobulin molecule which specifically binds to said preselected antigen or immunologically active fragment **of the antibody** [~~thereof~~], **said formulation obtained by processing plant cells** [~~wherein the immunoglobulin molecule is isolated from plant cells~~] containing nucleotide sequences encoding an immunoglobulin heavy chain polypeptide and an immunoglobulin light chain polypeptide wherein said nucleotide sequences also encodes a leader sequence for each polypeptide; and antigen specific immunoglobulin product encoded by said nucleotide sequences, wherein each leader sequence forms a secretion signal that is cleaved from each of said immunoglobulin heavy chain and light chain polypeptides following proteolytic processing.

41. (Amended) A method of passively immunizing a human or non-human animal subject against a preselected antigen, said method comprising administering to said subject a **formulation comprising a** prophylactic amount of an antigen-specific immunoglobulin, said [~~immunoglobulin isolated from~~] **formulation obtained by processing** plant cells containing nucleotide sequences encoding an immunoglobulin heavy chain and an immunoglobulin light chain wherein said nucleotide sequences also encode a leader sequence for said heavy chain and said light chain and wherein each leader sequence forms a secretion signal that is cleaved from each of said immunoglobulin heavy chain and light chain polypeptides following proteolytic processing.

66. (Amended) A method of passively immunizing a human or non-human animal subject against a preselected antigen, said method comprising administering to said subject a prophylactic amount of a **formulation comprising a** single polypeptide antigen-specific immunoglobulin, said [~~immunoglobulin isolated from~~] **formulation obtained by processing** plant cells, said plant cells containing nucleotide sequences encoding a single polypeptide comprising an immunoglobulin heavy chain and an immunoglobulin light chain wherein said nucleotide sequences also encode a leader sequence for said single

polypeptide wherein said leader sequence forms a secretion signal that is cleaved from said polypeptide following proteolytic processing.